

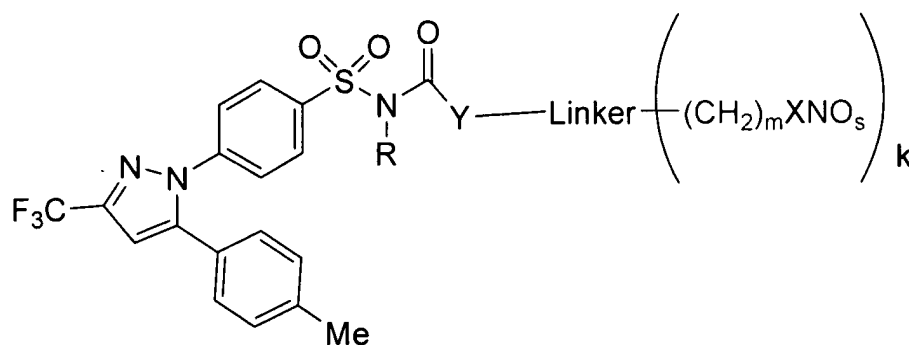
Amendments to the Claims:

This listing of claims replaces all prior versions, and listings, of claims in the application:

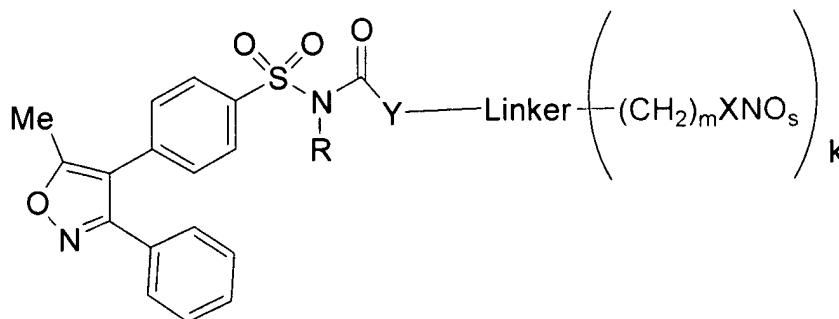
Listing of Claims:

1 to 12. (canceled)

13. (currently amended) A method of treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to ~~Claim 1~~ of Formula I or Formula II



Formula I



Formula II

or a pharmaceutically acceptable salt thereof, wherein

each s is independently 1 or 2;

k is 1, 2, 3 or 4;

each m is independently 0, 1, 2, 3 or 4;

each X is independently O or S;

Y is a bond, S, O or NR₁, wherein R₁ is hydrogen or C₁₋₆alkyl;

R is hydrogen or C₁₋₆alkyl;

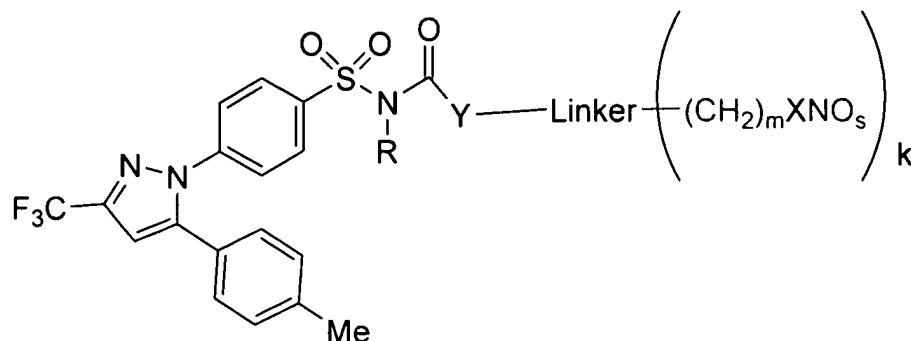
the Linker is selected from the group consisting of:

- (a) -(CH₂)_n, wherein n is 0, 1, 2, 3 or 4,
- (b) C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of
 - (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,
 - (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,
 - (8) CN;
 - (9) CH₂COOH
 - (10) CH₂COO-C₁₋₃alkyl,
 - (11) C₁₋₃alkthio,
- (c) aryl, wherein the aryl is selected from the group consisting of phenyl and naphthyl,
wherein the aryl is optionally mono-, di- or tri-substituted with a substituent
selected from the group consisting of
 - (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,
 - (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,

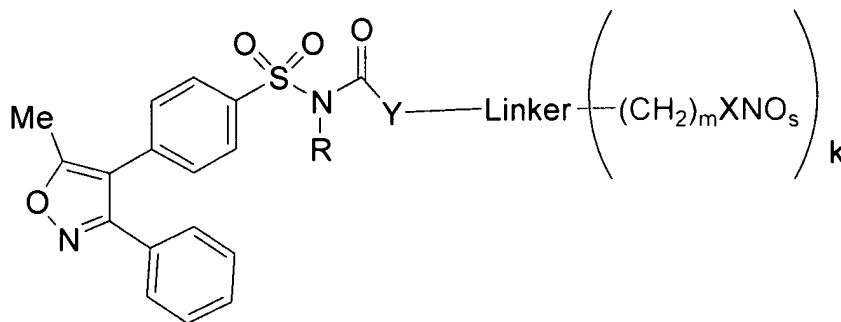
- (8) CN;
- (9) CH₂COOH
- (10) CH₂COO-C₁₋₃alkyl.
- (11) C₁₋₃alkthio.
- (d) Heteroaryl optionally mono-, di- or tri- substituted with substituents selected from the group consisting of
 - (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,
 - (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,
 - (8) CN;
 - (9) CH₂COOH
 - (10) CH₂COO-C₁₋₃alkyl,
 - (11) C₁₋₃alkthio.

14. (original) The method according to Claim 13 wherein the patient is also at risk of a thrombotic cardiovascular event.

15. (currently amended) A method of treating cyclooxygenase mediated diseases advantageously treated by an active agent that selectively inhibits COX-2 in preference to COX-1 comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound ~~according to Claim 1~~ of Formula I or Formula II



Formula I



Formula II

or a pharmaceutically acceptable salt thereof, wherein

each s is independently 1 or 2;

k is 1, 2, 3 or 4;

each m is independently 0, 1, 2, 3 or 4;

each X is independently O or S;

Y is a bond, S, O or NR₁, wherein R₁ is hydrogen or C₁-6alkyl;

R is hydrogen or C₁-6alkyl;

the Linker is selected from the group consisting of:

- (a) -(CH₂)_n, wherein n is 0, 1, 2, 3 or 4,
- (b) C₃-6cycloalkyl, wherein the C₃-6cycloalkyl optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of

- (1) halo,
- (2) C₁₋₃alkyl,
- (3) C₁₋₃alkoxy,
- (4) Hydroxy,
- (5) NO₂,
- (6) CO₂,
- (7) CF₃,
- (8) CN;
- (9) CH₂COOH
- (10) CH₂COO-C₁₋₃alkyl,
- (11) C₁₋₃alkthio,

(c) aryl, wherein the aryl is selected from the group consisting of phenyl and naphthyl, wherein the aryl is optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of

- (1) halo,
- (2) C₁₋₃alkyl,
- (3) C₁₋₃alkoxy,
- (4) Hydroxy,
- (5) NO₂,
- (6) CO₂,
- (7) CF₃,
- (8) CN;
- (9) CH₂COOH
- (10) CH₂COO-C₁₋₃alkyl,
- (11) C₁₋₃alkthio,

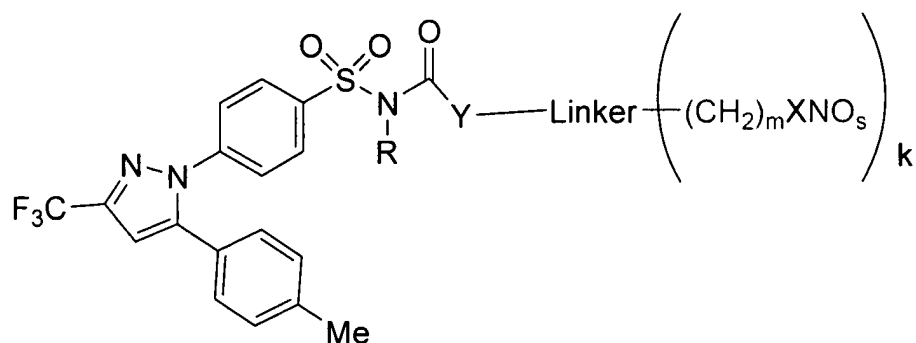
(d) Heteroaryl optionally mono-, di- or tri- substituted with substituents selected from the group consisting of

- (1) halo,
- (2) C₁₋₃alkyl,
- (3) C₁₋₃alkoxy,
- (4) Hydroxy,
- (5) NO₂,
- (6) CO₂,

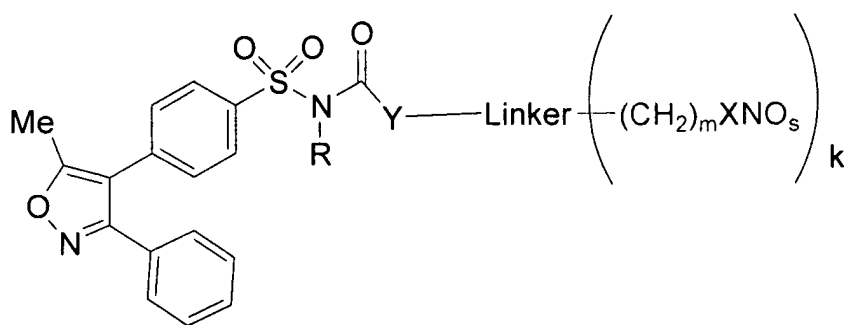
- (7) CF₃,
(8) CN;
(9) CH₂COOH
(10) CH₂COO-C₁₋₃alkyl,
(11) C₁₋₃alkthio.

16. (canceled)

17. (currently amended) A method for treating a chronic cyclooxygenase-2 mediated disease or condition and reducing the risk of a thrombotic cardiovascular event in a human patient in need of such treatment and at risk of a thrombotic cardiovascular event comprising orally concomitantly or sequentially administering to said patient a compound according to ~~Claim 1~~ of Formula I or Formula II



Formula I



Formula II

or a pharmaceutically acceptable salt thereof, wherein

each s is independently 1 or 2;

k is 1, 2, 3 or 4;

each m is independently 0, 1, 2, 3 or 4;

each X is independently O or S;

Y is a bond, S, O or NR₁, wherein R₁ is hydrogen or C₁₋₆alkyl;

R is hydrogen or C₁₋₆alkyl;

the Linker is selected from the group consisting of:

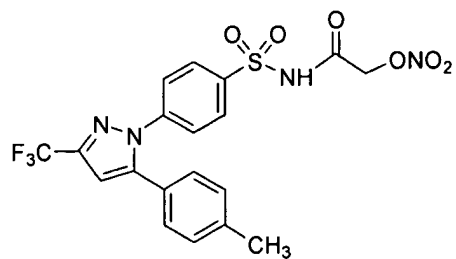
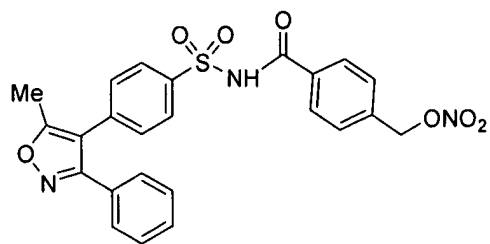
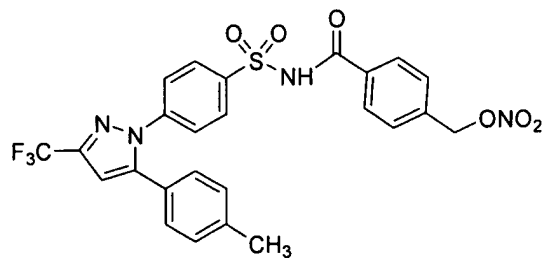
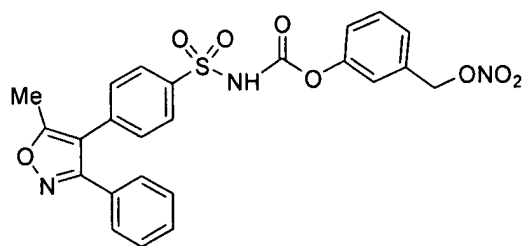
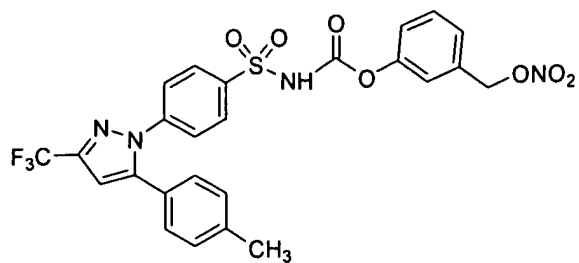
- (a) -(CH₂)_n, wherein n is 0, 1, 2, 3 or 4,
- (b) C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of
 - (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,
 - (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,
 - (8) CN;
 - (9) CH₂COOH
 - (10) CH₂COO-C₁₋₃alkyl,
 - (11) C₁₋₃alkthio,
- (c) aryl, wherein the aryl is selected from the group consisting of phenyl and naphthyl, wherein the aryl is optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of
 - (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,

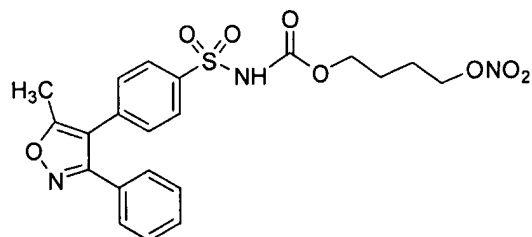
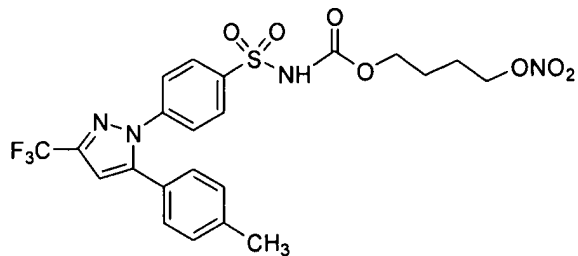
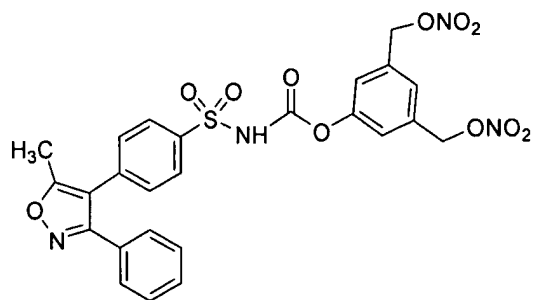
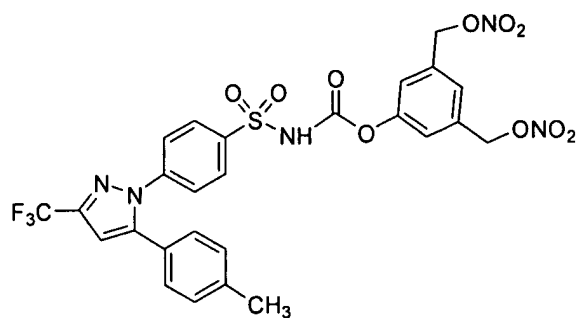
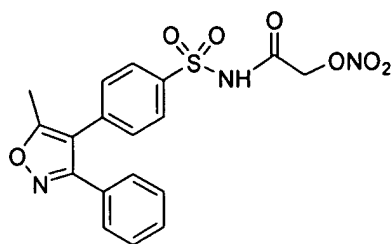
- (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,
 - (8) CN;
 - (9) CH₂COOH
 - (10) CH₂COO-C₁₋₃alkyl,
 - (11) C₁₋₃alkthio,
- (d) Heteroaryl optionally mono-, di- or tri- substituted with substituents selected from the group consisting of
- (1) halo,
 - (2) C₁₋₃alkyl,
 - (3) C₁₋₃alkoxy,
 - (4) Hydroxy,
 - (5) NO₂,
 - (6) CO₂,
 - (7) CF₃,
 - (8) CN;
 - (9) CH₂COOH
 - (10) CH₂COO-C₁₋₃alkyl,
 - (11) C₁₋₃alkthio,

in an amount effective to treat the cyclooxygenase-2 mediated disease or condition and aspirin in an amount effective to reduce the risk of the thrombotic cardiovascular event.

18. to 26. (canceled)

27. (currently amended) ~~A compound~~ The method according to Claim 17 wherein the compound is selected from the following group:





Serial No.: 10/530,214
Case No.: MC072P
Page 12

or a pharmaceutically acceptable salt of any of the foregoing compounds.

28. (canceled)